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Brief Communication

Diagnostic value of the REM sleep behavior disorder screening questionnaire in Parkinson's disease

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ABSTRACT

Objective: We aimed to validate the rapid eye movement (REM) sleep behavior disorder (RBD) screening questionnaire (RBDSQ) in 2 independent samples of patients with Parkinson's disease (PD) using different settings when performing the investigations.
Methods: The RBDSQ was administered to two independent samples of 52 and 75 consecutive PD patients investigated with video-polysomnography (vPSG).
Results: In sample A, the RBDSQ identified 46/52 (88.5%) patients correctly. In sample B, 50/75 (66.7%) patients were identified correctly. Considering a cut-off score of ≥ 5 as a positive test result, sample A showed a sensitivity of 0.90 and a specificity of 0.87, sample B showed a sensitivity of 0.68 and a specificity of 0.63. Main differences between both groups were that patients of sample A underwent a sleep history including RBD assessment prior to administration of the RBDSQ, whereas in sample B the RBDSQ was administered during routine work-up.
Conclusions: The diagnostic value of the RBDSQ strongly depends on the clinical setting and may be influenced by the individual's awareness on RBD. This finding is a critical issue which deserves clarification before use of this and other questionnaires can be recommended in epidemiological studies.

1. Introduction

Rapid eye movement (REM) sleep behavior disorder (RBD) is clinically characterized by the intermittent loss of physiological skeletal muscle atonia during REM sleep with the appearance of elaborate motor activity associated with dream mentation [1]. Apart from the characteristic clinical picture, polysomnography (PSG) demonstrating REM sleep without atonia is required for establishing a definite diagnosis of RBD [2]. The RBD screening questionnaire (RBDSQ) was developed and validated to meet the need for an easily applicable and short diagnostic screening tool [3]. It was shown to have a high sensitivity for RBD in both sleep-disorder patients and healthy controls [3]. Up to 46% of Parkinson's disease (PD) patients have RBD [4–6]. Since the usefulness of the RBDSQ in PD is still controversial [7–9], we aimed to validate the RBDSQ in 2 independent samples of PD patients using different settings when performing the investigations.

2. Methods

2.1. Patient samples and procedures

All patients in this study were referred to video-PSG (vPSG) at the sleep laboratory of Innsbruck University or at the Paracelsus-Elena-Klinik Kassel because of reported sleep disturbances, and underwent single or multiple night v-PSG according to clinical considerations. The RBDSQ [3] was completed prior to vPSG.

All patients analyzed in this study consented to scientific evaluation of their clinical data. The Ethical Committee of the Landesärztekammer Hessen agreed to the project.

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Patient sample A was specifically selected to validate the RBDSQ in PD. It consisted of 52 consecutive PD patients (23 Innsbruck, 29 Kassel) who underwent a sleep history including assessment of the presence of RBD prior to administration of the RBDSQ. Sixty-two percent of patients underwent one night v-PSG, 38% had multiple night vPSG. RBD was diagnosed according to the criteria of the International Classification of Sleep Disorders, 2nd revision (ICSD-2) [2] based on (1) a history suggestive of RBD or presence of clear dream-enacting behaviors during REM sleep documented on vPSG, and (2) a qualitative finding of REM sleep without atonia in the video-polysomnography defined as presence of an excessive amount of phasic or tonic EMG activity in the chin or extremity muscles following the recommendations of the American Academy of Sleep Medicine.

Patient sample B consisted of 75 PD patients (75 Kassel) in whom the RBDSQ was administered during routine work-up without prior interview on possible RBD. Eighty-three percent of patients underwent one night of v-PSG, 17% had multiple night v-PSG. RBD was diagnosed according to the criteria of the ICSD-2 [2] based on (1) the presence of clear dream-enacting behaviors during REM sleep documented on vPSG, and (2) a qualitative finding of REM sleep without atonia in the vPSG defined as presence of an excessive amount of phasic or tonic EMG activity in the chin or extremity muscles following the recommendations of the American Academy of Sleep Medicine. Vocalizations during REM sleep alone were not sufficient to be rated as dream enacting behavior.

2.2. Statistical analysis

In case of normal distribution, data were given as mean values (±standard deviation) and independent t-tests were applied; in case of non-normal distribution, median values (range) were given and Mann–Whitney tests were calculated. For categorical variables, Fisher's exact test was applied. The diagnostic value of the RBDSQ was calculated by the area under the curve (AUC). The primary outcome measures were to evaluate if a cut-off score of 5 is appropriate for RBD screening in PD, and if the RBDSQ is suitable for RBD detection in subjects without prior information on RBD, as this most likely reflects the typical situation in epidemiologic studies. A p-value < 0.05 was considered significant.

3. Results

3.1. Clinical characteristics (Table 1)

3.1.1. Patient sample A

Patient sample A consisted of 52 PD patients of whom 37 subjects (71.2%) had RBD and 15 (28.8%) had no RBD. PD patients with and without RBD differed in the rate of selective serotonin reuptake (SSRI) or serotonin-norepinephrine reuptake inhibitor (SNRI) use (RBD-PD vs. Non-RBD-PD: 17 (46%) vs. 1 (7%), p = 0.009). No differences were found for sex (RBD-PD vs. Non-RBD-PD: 20 men (54%) vs. 6 (40%), p = 0.541), age (67 ± 8 vs. 65 ± 7, p = 0.505), disease duration (7 (1–30) vs. 4 (1–10), p = 0.180), H&Y stage (3 (1–5) vs. 3 (1–3), p = 0.542), sleep-related breathing disorder [SRBD (RBD-PD vs. Non-RBD-PD: 17 SRBD (46%) vs. 6 (40%), p = 0.542)], levodopa dosage (450 (0–1400) vs. 400 (0–1000) mg/day, p = 0.590), and dopamine agonist equivalent dosage (100 (0–2000) vs. 175 (0–2400) mg/day, p = 0.548).

3.1.2. Patient sample B

Patient sample B consisted of 75 PD patients. Sex, age, disease duration, H&Y stage, SRBD, and dopamine agonist equivalent dosage were comparable to sample A, whereas levodopa dosage was higher and use of SSRIs or SNRIs was lower in patient sample B. 56 patients (75%) were identified with RBD, 19 (25%) had no RBD. Both groups did not differ in sex (39 men (69.6%) vs. 11 men (64.7%), p = 0.348), age (RBD-PD vs. Non-RBD-PD: 67 (48–77) vs. 67 (65–71) years, p = 0.380), disease duration (7 ± 5 vs. 8 ± 6 years, p = 0.726), H&Y stage (3 (2–5) vs. 3 (3–4), p = 0.937), SRBD (RBD-PD vs. Non-RBD-PD: 16 SRBD (29%) vs. 6 (32%), p = 1.000), levodopa dosage (753 (200–1800) vs. 580 (40–1043) mg/day, p = 0.699), dopamine agonist equivalent dosage (200 (50–840) vs. 185 (50–400) mg/day, p = 0.550), and SSRI/SNRI intake (RBD-PD vs. Non-RBD-PD: 6 SRBD (11%) vs. 4 (20%), p = 0.442).

Table 1
Clinical characteristics of both investigated patient samples.

Demographics	Patient sample A (n = 52)	Patient sample B (n = 75)	p-value
Age, y	69 (46–83)	67 (48–77)	0.837[a]
Gender, m (%)	26 (50)	50 (67)	0.068[b]
Disease duration, y	5 (1–30)	8 (2–20)	0.248[a]
H&Y stage	3 (1–5)	3 (2–5)	0.263[a]
LD dose mg/day	413 (0–1400)	730 (200–1800)	<0.001[a]
DA dose mg/day	102 (0–2400)	200 (50–840)	0.248[a]
SSRI/SNRI intake, n (%)	18 (35)	10 (13)	0.008[b]
Cholinesterase inhibitor intake, n (%)	1 (2)	0 (0)	N.A.
Benzodiazepine intake*, n (%)	3 (6)	8 (11)	0.523[b]
SRBD, n (%)	23 (44)	22 (29)	0.084[b]
Mild (AHI 5–15/h), n (%)	15 (29)	13 (17)	
Moderate (AHI 15–30/h), n (%)	3 (6)	5 (7)	
Severe (AHI > 30/h), n (%)	5 (10)	4 (5)	
RBD, n (%)	37 (71)	56 (75)	0.688[b]
RBDSQ score	6 (0–12)	6 (0–11)	0.364[a]

Legend. All values are given as median (range) or frequencies (percentages).
Abbrevations: y, years; m, men; H&Y stage, Hoehn and Yahr stage; LD, levodopa; DA, dopamine agonist equivalent dosage as calculated according to Möller et al. J Neurol 2005; RBDSQ score, REM sleep behavior disorder screening questionnaire score; SNRI, serotonin-norepinephrine reuptake inhibitors; SRBD, sleep-related breathing disorder; SSRI, selective serotonin reuptake inhibitors.
[a] Based on Mann–Whitney test.
[b] Based on Fisher's exact test (2-sided).
* No patient received treatment for RBD at time of video-polysomnography.

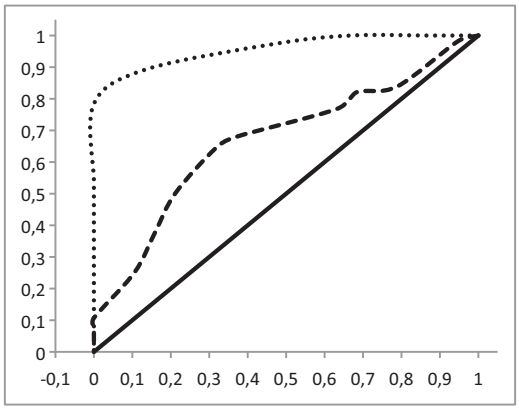

Fig. 1. Sensitivity and specificity of the RBDSQ scores as shown by a ROC curve with a cut-off of 5 for patients of sample A and sample B.
Legend. Note that the RBDSQ proved to be useful when clinical information on RBD was provided (sample A, dotted line). However, it proved to be less useful when the RBDSQ was implemented in the routine work-up with no specific assessment of RBD prior to filling out the RBDSQ (sample B, broken line).

3.2. RBDSQ (Fig. 1)

3.2.1. Patient sample A

The mean RBDSQ score in the RBD-PD group was 7.5 ± 2.4 points compared with 3.1 ± 1.4 points in the Non-RBD PD group ($p < 0.001$). Thirty-five of the 52 patients PD patients showed a RBDSQ score >5. Of these 35 patients, 33 were identified with RBD in vPSG. Seventeen of the 52 patients PD patients showed a RBDSQ score <5 points as a negative test result. Of these 17 negative patients, 4 were identified with RBD in vPSG. Considering a RBDSQ score of 5 points as a positive test result as indicated in idiopathic RBD we found a sensitivity of 0.90 and a specificity of 0.87. Forty-six (88.5%) of the patients were correctly diagnosed. The AUC was 0.95 with a 95% confidence interval of 0.90–1.0 and compared with the minimum possible score of 0.5 the difference was highly significant ($p < 0.001$). The optimal cut-off value which was defined as highest sum of sensitivity and specificity was 6. By using this cut-off value, sensitivity considerably decreased to 0.78, while specificity reached 1.00. Forty-eight (92.3%) of the patients were correctly diagnosed.

3.2.2. Patient sample B

In this group, the mean RBDSQ score in the RBD-PD group was 6.0 ± 3.1 points compared with 4.2 ± 2.7 points in the Non-RBD PD group ($p < 0.05$). A RBD-SQ score >5 was found in 45/75 PD patients. Considering a RBDSQ score of > 5 points as a positive test result, 38/45 patients with a RBDSQ score above the cut-off value were identified with RBD in vPSG and 7/45 had no RBD. 30/75 PD patients showed a RBDSQ score <5 points as a negative test result. In this group 18 patients were identified with RBD in vPSG. Sensitivity was calculated at 0.68 and specificity at 0.63. Accordingly, 50/75 (66.7%) of the patients were correctly diagnosed. The AUC was 0.67 with a 95% confidence interval of 0.54–0.80 and compared with the minimum possible score of 0.5 the difference was significant ($p = 0.029$). By using the optimal cut-off value of 6 points, 39 of the 75 patients (52%) were correctly identified by the RBDSQ and sensitivity decreased to 0.64, while specificity increased to 0.68.

4. Discussion

This study evaluated the diagnostic value of the RBDSQ in two samples of PD patients, and found substantial and surprising differences of sensitivity and specificity between both samples: whereas sensitivity and specificity were high in sample A, they were at best moderate in sample B.

Which factors might potentially account for this discrepancy? First, sample A consisted of PD patients who had a sleep interview including RBD assessment prior to the RBDSQ, which alerted the patients about RBD as a disease associated with nocturnal behaviors. Sample B, however, were routine patients in whom the RBDSQ was administered during regular work-up and in whom the preceding clinical interview asked about non-motor symptoms and sleep in general, but not specifically on RBD. Accordingly, sensitivity and specificity of the RBDSQ in sample A paralleled the findings of the original RBDSQ validation study [3], in which the questionnaire was applied to patients who were aware of their RBD status. This, however, is a critical issue when validating a questionnaire with the aim to use it as screening tool in large patient- or population-based studies. In this light, results of other RBD questionnaires should be interpreted with caution [10–13]. Indeed, a single question screener for RBD [10] was validated in RBD patients who participated in a study aiming at RBD environmental risk factors [14] and hence were aware of RBD. The high sensitivity and specificity of the single question is therefore not surprising.

Second, criteria for a diagnosis of RBD were chosen slightly differently between sample A and B. Apart from REM sleep without atonia in the PSG the presence of either a history or clear dream enacting behaviors during REM sleep in the video were sufficient for a diagnosis of RBD in sample A, whereas diagnosis of RBD in sample B was based solely on vPSG information without consideration of a positive or negative RBD history. This could have led to an increased number of false negatives in sample B, since these patients were not necessarily aware of nocturnal motor behaviors. However, our data showed that there were also more non-RBD patients who were classified falsely as RBD positives which argues against a strong influence of the modified diagnostic criteria on the divergent results. Similar conclusions can be drawn from differences in nights of v-PSG investigation between both groups. As the number of investigated nights was based on the individual clinical need, and RBD does not completely disappear in intensity from night to night [15], we do not think that this difference explains our results.

Third, use of SSRI/SNRI differed between both samples, with more patients in sample A being on current SSRI/SNRI medication. Although the total number of patients with RBD was similar between both groups, we cannot exclude that use of SSRI/SNRI in sample A led to more severe RBD which might be potentially better captured with the RBDSQ. In addition, although not significant, patient sample A had a higher proportion of men compared to patient sample B. As men were reported to exhibit more violent behaviors than women during RBD episodes [16], it might be tempting to speculate that RBD questionnaires might be more effective in men than in women due to their different clinical presentation. This, however, awaits further investigation.

Our findings further corroborate the notion that a questionnaire can be at best a screening tool which will not reach the diagnostic level of vPSG as the gold standard for RBD diagnosis. Only vPSG can reliably rule out important differential diagnoses [2,17–19]. A significant number of “true” RBD cases will be missed by clinical interview alone [20,21], whereas the number of false positives according to questionnaires alone is considerable even in healthy sleepers in whom RBD was later carefully excluded by expert interview and v-PSG [22].

All PD patients completed the RBDSQ at the time of PSG without immediate input of the bedpartner. Additional input of a bedpartner could have led to a higher sensitivity and specificity. On the other hand, the results of our study reflect real-life conditions in clinical routine, especially in elderly PD patients, where often a bedpartner is no longer available.

Our study demonstrates that the diagnostic value of the RBDSQ strongly depends on the clinical setting, and may be influenced by the individual's awareness on RBD. This finding is a critical issue which deserves clarification before use of this and other questionnaires can be recommended in epidemiological studies.

Conflict of interest

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: http://dx.doi.org/10.1016/j.sleep.2014.08.014.

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